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CONFORMATIONAL ANALYSIS OF SUBSTITUTED 1,3,2-OXAZABORINANES

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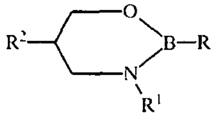
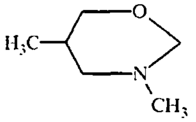
The empirical (MM2) and semiempirical (AM1, MNDO) methods were used to calculate the energy of unsubstituted and 2-, 3-, 5-, 3,5-, and 2,3,5-substituted 1,3,2-oxazaborinanes with complete geometrical optimization. The major minimum on the potential energy surface corresponds to the sofa conformation. The number of other local minima relates to the half-chair and 1,4-, 3,6-, and 2,5-twist conformations. The experimental ΔG^0 *value for 5-methyl group on the* $C_{(5)}$ *carbon atom was determined by comparisom of calculated and experimental spin-spin coupling constants.*

The flattened character of the predominant conformation for cyclic borate esters is largely dictated by the partial double bond character of the boron–heteroatom bond [1]. On the other hand, the conformational equilibrium of substituted 1,3,2-oxazaborinanes, which are interesting asymmetrical six-membered heterocycles with three heteroatoms, features a more significant contribution of the flexible forms in comparison with their oxygen analogs, namely, 1,3,2-dioxaborinanes. Kalyuskii et al. [2-6] has shown that, depending on the number and location of the alkyl substituents, conformers or invertomers of the sofa and one of the twist forms may predominate for 1,3,2-oxazaborinanes. However, quantitative evaluation of the relative stability of these forms using the CNDO method is difficult as in the case of 1,3,2-dioxaborinanes [1, 7] due to the imprecise description of the electronic interactions in the heteroatomic fragment [8, 9].

In the present work, we calculated the energy and three-dimensional structure of the possible conformers of a series of 1,3,2-oxazaborinanes (I–VII) and model 3,5-dimethyltetrahydro-1,3-oxazine (VIII) by the molecular mechanics MM2 [10], LCAO MO SCF AM1 [11, 12] and MNDO methods [13, 14] with complete geometrical isomerization.


I–VII


VIII

I $R = R^1 = R^2 = H$; II $R = CH_3$, $R^1 = R^2 = H$; III $R = R^2 = H$, $R^1 = CH_3$; IV $R = R^1 = H$, $R^2 = CH_3$;
V $R = H$, $R^1 = R^2 = CH_3$; VI $R = R^2 = CH_3$, $R^1 = C_6H_{11}$; VII $R = R^2 = CH_3$, $R^1 = CH_2C_6H_5$

A number of minima corresponding to the sofa conformer (S), two half-chair forms (HC-1 and HC-2), and 1,4-, 3,6-, and 2,5-twist forms (1,4-T, 3,6-T, and 2,5-T) were found on the potential energy surface for all the cyclic borate esters studied.

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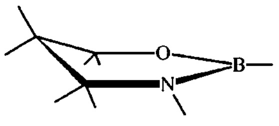
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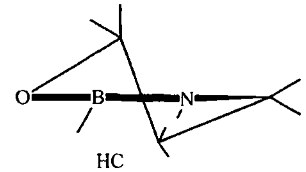
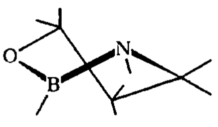
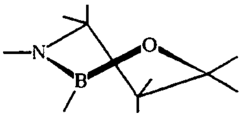
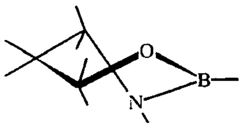

HC


1.4-T


3.6-T

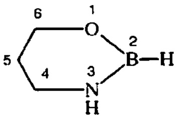

2.5-T

All the forms with the exception of S were obtained by fixing the C^{4}NBO and C^{6}OBN torsion angles. Otherwise, these forms would isomerize into the sofa. Even with these restrictions, conformer 2,5-T converts to the half-chair during minimization in the MNDO and AM1 calculations.

The torsion angles of the most stable conformers given in Table 1 suggest that HC-1 and HC-2 differ in the extent of deformation of the C^{4}NBO and C^{6}OBN fragments. We should also note the considerable flattening of the sofa given by the MNDO calculation in comparison with the MM2 and AM1 results. The calculated bond lengths and angles of this form correspond to the experimental data for oxygen- and nitrogen-containing organoboron heterocycles [15, 16].

The relative energies for the conformers of compounds I–VIII are given in Table 2. The S form for cyclic borate esters (sofa form with an equatorial substituent at $C_{(5)}$ for 5-, 2,5- and 2,3,5-substituted derivatives, Se) is most stable, which is in complete accord with the experimental data [3, 17]. The differences in energy with the alternative forms within the error margin of the calculation (±0.01 kcal/mole) range from 0.1 (HC-1) to 7.4 kcal/mole ((2,5-T by the MM2 method). In the case of esters I–IV, independent of the nature of the substituent at the boron atom (H or CH$_3$), the stability of the conformers decreases in the following series: Se ≥ HC-1e > HC-2e > Sa > HC-1a > HC-2a > 1,4-T > 3,6-T > 2,5-T. The AM1 calculation in almost all cases leads to degenerate values of the energy for conformers S (or Se) and HC-1 (or HC-1e). PMR spectroscopy showed that 2- and 2,3-substituted 1,3,2-oxazaborinanes exist in equilibrium between two inverted sofa forms with a rather low barrier between them [3]. Inversion of such systems presumably proceeds through half-chair and, probably, 1,4- and 3,6-twist forms.

TABLE 1. Internal Torsion Angles (deg) for Individual Conformers of Ester I



Calculation	Conformer	1-2-3-4	2-3-4-5	3-4-5-6	4-5-6-1	5-6-1-2	6-1-2-3
MM2	S	-3.7	26.0	-51.0	55.6	-34.6	8.3
	HC-1	-2.5	-19.8	51.4	-61.4	38.0	-7.4
	HC-2	-7.4	36.6	-60.0	52.6	-21.2	-1.3
AM1	S	-2.6	-17.2	42.4	-51.1	32.6	-5.4
	HC-1	-4.3	-13.8	40.5	-52.4	35.8	-7.2
	HC-2	-6.2	30.5	-47.6	43.4	-19.7	-0.2
MNDO	S	-0.4	-16.3	33.4	-37.4	22.3	3.4
	HC-1	-3.9	-8.6	29.5	-40.1	29.1	-7.1
	HC-2	-7.4	27.1	-37.3	30.8	-10.6	-2.0

Conformer Se of molecules IV–VII is more stable than the axial form, Sa, by 0.7-1.2 kcal/mole. On the other hand, the calculated energy differences between the chair forms Ce and Ca of oxazine VIII vary from 0.5 (MNDO) to 1.1 kcal/mole (MM2), which is 9-40% lower than the corresponding data for the cyclic borate esters. This behavior probably results from a difference in the orientation of the *n*-electron pairs of the oxygen and nitrogen atoms in the borate esters due to conjugation with the vacant boron orbital, which enhances the nonbonding interactions of the axial alkyl group at $C_{(5)}$ with the heteroatom fragment in the sofa conformation [1, 3, 17]. We compared the actual and calculated geometries of 5-methyl-1,3,2-oxazaborinanes IV–VII using the experimental [3] and calculated vicinal coupling constants. The calculated constants were obtained using the torsion angles between the corresponding protons, the following equation [18], and electronegativity data [19]:

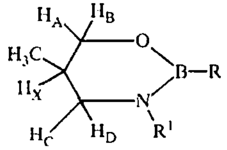
$$^{3}J_{HH} = (7.8 - \cos\varphi + 5.6\cos2\varphi)(1 - 0.1\Sigma\Delta\chi_i)\ [18],$$

where $\Delta\chi_i$ is the difference in the electronegativities of the substituent atom in the ethane fragment examined and hydrogen.

TABLE 2. Relative Energies (kcal/mole) for Conformers of Compounds I–VIII

Compound	Conformer	MM2		AM1		MNDO	
		E	Δ*E*	-*E*	Δ*E*	-*E*	Δ*E*
I	S	2.8	0.0	1334.5	0.0	1333.2	0.0
	HC-1	3.1	0.3	1334.4	0.1	1333.0	0.2
	HC-2	3.2	0.4	1333.6	0.9	1332.8	0.4
	1,4-T	4.9	2.1	1332.5	2.0	1331.9	1.3
	3,6-T	5.8	3.0	1331.3	3.2	1331.5	1.7
	2,5-T	9.0	6.2	—	—	—	—
II	S	1.4	0.0	1621.0	0.0	1623.8	0.0
	HC-1	1.6	0.2	1621.0	0.0	1623.6	0.2
	HC-2	1.7	0.3	1620.1	0.9	1623.4	0.4
	1,4-T	3.3	1.9	1619.3	1.7	1622.6	1.2
	3,6-T	4.2	2.8	1618.0	3.0	1622.3	1.5
	2,5-T	7.4	6.0	—	—	—	—
III	S	3.8	0.0	1602.4	0.0	1604.6	0.0
	HC-1	3.9	0.1	1602.4	0.0	1604.4	0.2
	HC-2	4.3	0.5	1601.6	0.8	1604.3	0.3
	1,4-T	6.0	2.2	1600.4	2.0	1603.1	1.5
	3,6-T	6.8	3.0	1599.3	3.1	1603.1	1.5
	2,5-T	10.3	6.5	—	—	—	—
IV	Se	3.3	0.0	1614.9	0.0	1610.1	0.0
	Sa	4.5	1.2	1614.0	0.9	1609.4	0.7
	HC-1e	3.5	0.2	1614.9	0.0	1609.9	0.2
	HC-2e	3.7	0.4	1614.0	0.9	1609.6	0.5
	HC-1a	4.8	1.5	1613.9	1.0	1609.2	0.9
	HC-2a	4.9	1.6	1613.1	1.8	1608.9	1.2
	1,4-T	5.5	2.2	1612.8	2.1	1608.4	1.7
	3,6-T	6.3	3.0	1611.5	3.4	1608.0	2.1
	2,5-T	10.7	7.4	—	—	—	—
V	Se	4.2	0.0	1882.9	0.0	1881.5	0.0
	Sa	5.4	1.2	1881.9	1.0	1880.8	0.7
VI	Se	16.1	0.0	3460.6	0.0	3450.4	0.0
	Sa	17.1	1.0	3459.5	1.1	3449.6	0.8
VII	Se	-0.8	0.0	3375.3	0.0	3373.4	0.0
	Sa	0.4	1.2	3374.2	1.1	3372.7	0.7
VIII	Ce	9.0	0.0	1924.1	0.0	1922.5	0.0
	Ca	10.1	1.1	1923.1	1.0	1922.0	0.5

TABLE 3. Torsion Angles between Protons (deg) and Coupling Constants (Hz) for Individual Conformers of Compounds IV–VII



Compound	Calculation method	Conformer	φ_{AX}	φ_{BX}	φ_{CX}	φ_{DX}	$^3J_{AX}$	$^3J_{BX}$	$^3J_{CX}$	$^3J_{DX}$	ΣJ	$\lvert\Delta\Sigma J\rvert$*
1	2	3	4	5	6	7	8	9	10	11	12	13
IV	MM2	Se	179.7	57.4	171.1	56.7	11.4	3.9	12.0	4.2	31.5	1.0
		Sa	56.7	65.1	54.0	65.9	4.0	3.0	4.6	3.1	14.7	15.8
	AM1	Se	172.6	51.3	163.6	46.8	11.2	4.7	11.2	5.6	32.7	2.2
		Sa	46.3	74.9	37.9	78.8	5.4	2.1	7.0	2.0	16.5	14.0
		HC-1e	173.9	52.3	161.8	45.2	11.3	4.6	11.1	5.9	32.9	2.4
		HC-1a	47.6	73.7	36.0	80.6	5.2	2.2	7.3	2.0	16.7	13.8
		HC-2e	165.2	44.5	168.2	51.1	10.8	5.7	11.6	5.0	33.1	2.6
		HC-2a	38.8	81.6	42.4	74.5	6.5	1.8	6.3	2.3	16.9	13.6
	MNDO	Se	162.0	45.1	158.8	42.2	10.5	5.6	10.7	6.4	33.2	2.7
		Sa	34.0	81.9	30.3	85.3	7.2	1.8	8.1	1.8	18.9	11.6

TABLE 3 (continued)

1	2	3	4	5	6	7	8	9	10	11	12	13
V	MM2	Se	179.2	58.4	175.9	56.6	11.4	3.8	12.0	4.2	31.4	0.9
		Sa	57.6	64.2	53.0	65.7	3.9	3.1	4.7	3.1	14.8	15.7
	AM1	Se	173.2	51.6	165.1	48.3	11.2	4.7	11.4	5.4	32.7	2.2
		Sa	46.7	74.7	39.2	77.4	5.4	2.1	6.8	2.1	16.4	14.1
	MNDO	Se	162.6	45.3	162.3	46.3	10.5	5.6	11.1	5.7	32.9	2.5
		Sa	34.3	82.0	33.9	81.0	7.2	1.8	7.6	1.9	18.5	12.0
VI	MM2	Se	176.8	60.1	174.4	55.7	11.3	3.5	11.9	4.3	31.0	0.5
		Sa	59.9	62.7	51.7	66.4	3.6	3.2	4.9	3.0	14.7	15.8
	AM1	Se	175.2	53.4	165.0	46.6	11.3	4.4	11.4	5.7	32.8	2.3
		Sa	48.3	73.2	39.0	77.2	5.1	2.2	6.8	2.1	16.2	14.3
	MNDO	Se	161.8	44.4	167.8	52.8	10.5	5.7	11.6	4.8	32.6	2.1
		Sa	33.6	82.9	37.8	76.0	7.2	1.8	7.0	2.2	18.2	12.3
VII	MM2	Se	177.9	59.3	175.4	56.6	11.4	3.6	12.0	4.2	31.2	0.7
		Sa	58.9	62.3	52.5	65.8	3.7	3.2	4.8	3.1	14.8	15.7
	AM1	Se	174.3	52.7	166.3	49.7	11.3	4.5	11.5	5.2	32.5	2.0
		Sa	47.3	74.0	40.2	76.3	5.3	2.2	6.7	2.2	16.4	14.1
	MNDO	Se	164.2	46.7	163.8	48.3	10.7	5.4	11.3	5.4	32.8	2.3
		Sa	35.1	81.3	35.3	79.1	7.0	1.8	7.4	2.0	18.2	12.3

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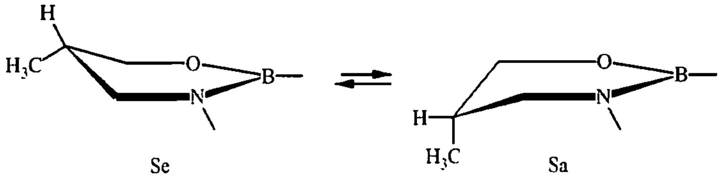
* $|\Delta\Sigma J| = |\Sigma J_{\mathrm{exp}} - \Sigma J_{\mathrm{calc}}|$. Experimental coupling constants [3]: for compounds IV, V, and VII $^3J_{AX} = 10.2$, $^3J_{BX} = 5.2$, $^3J_{CX} = 10.5$, $^3J_{DX} = 4.6$ Hz ($\Sigma J = 30.5$ Hz); for compound VI $^3J_{AX} = 9.8$, $^3J_{BX} = 4.6$, $^3J_{CX} = 10.2$, $^3J_{DX} = 4.2$ Hz, $\Sigma J = 28.8$ Hz.

The results given in Table 3, in particular, the sums of the calculated and experimental coupling constants, unequivocally indicate predominance of the Se conformer for esters IV–VII. The discrepancies between the calculated and experimental coupling constants of this form ranging from 0.5 to 2.5 Hz ($|\Delta\Sigma J|$) are related in part to the imperfect parameter selection [18] and incomplete consideration of the intramolecular interactions due to lack of a correction for the effect of the medium (in each case, an isolated molecule in vacuum was examined). However, the major reason for these discrepancies is the lack of conformational uniformity of molecules IV–VII due to the contribution of conformers with $\Delta E \leq 1.2$ kcal/mole, namely, HC-1e, HC-2e, and Sa; the other forms may be ignored in light of high ΔE values (Table 2). The calculated coupling constants of conformer Se and the equatorial half-chair forms found for ester IV using the optimal geometry obtained in the AM1 calculation differ, on the average, by not more than 0.2-0.6 Hz (Table 3). Hence, the conformational state of 5-methyl derivatives IV–VII may be represented rather accurately as an equilibrium mixture:



An approach based on comparing the mean weighted experimental and standard coupling constants [20] was used to evaluate the equilibrium of this system:

$$\Sigma\, {}^3J_{\mathrm{exp}} = N(\Sigma\, J_{\mathrm{aa}}, J_{\mathrm{ae}}) + (1 - N)(\Sigma\, J_{\mathrm{ea}}, J_{\mathrm{ee}}).$$

The calculated constants for conformers Se (N) and Sa ($1 - N$) were used as the standards. The results obtained shown in Table 4 indicate that the mean ΔG^0 at 293°K is 1.1 kcal/mole in favor of form Se (this value is close to the results of the MM2 and AM1 calculations). In selecting the standard coupling constants from the PMR spectra of the *cis* and *trans* isomers of 4,5-dimethyl-1,3,2-oxazaborinanes [4], the ΔG^0 value of the methyl group at $C_{(5)}$ is 1.0-1.2 kcal/mole [17]. Thus, taking account of the noted approximations, the value found for the free conformational energy probably reflects the actual extent of nonbonding repulsion between the methyl group and lone electron pairs of the heteroatoms in the cyclic borate esters.

TABLE 4. Parameters of the Se and Sa Conformational Equilibrium for Compounds IV–VII

Compound	Calculation method	N	K_{eq}	ΔG^0*	ΔG^0_{av}
IV	MM2	0.94	15.67	1.60	1.1
	AMI	0.86	6.14	1.06	
	MNDO	0.81	4.26	0.84	
V	MM2	0.95	19.00	1.71	
	AMI	0.87	6.69	1.10	
	MNDO	0.83	4.88	0.92	
VI	MM2	0.87	6.69	1.10	
	AMI	0.76	3.17	0.67	
	MNDO	0.74	2.85	0.61	
VII	MM2	0.96	24.00	1.85	
	AMI	0.88	7.33	1.16	
	MNDO	0.84	5.25	0.96	

$$\Delta G^0 = -RT \ln \frac{N}{1-N}.$$

These results substantially expand the data base for the stereochemistry of substituted 1,3,2-oxazaborinanes and open possibilities for prediction of the conformational state of such molecules.

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